EXHIBIT H

Continued Access to Investigational Devices During PMA Preparation and Review July 15, 1996 (D96-1)

See Related Information

This guidance was written prior to the February 27, 1997 implementation of FDA's Good Guidance Practices, GGP's. It does not create or confer rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. This guidance will be updated in the next revision to include the standard elements of GGP's.

IDE Memorandum - #D96-1

Office of Device Evaluation (HFZ-400)

Continued Access to Investigational Devices During
PMA Preparation and Review

ODE Review Staff

Purpose

The purpose of this memorandum is to adopt an official policy on the continued access to investigational devices while a marketing application is being prepared or reviewed.

Policy

On May 10, 1995, the Office of Device Evaluation issued a memorandum to the ODE review staff explaining the conditions under which an

investigational device may be made available during the preparation or review of a marketing application.

Under this policy, a sponsor may propose to conduct an "extended" clinical trial if: 1) there is a public health need for the device and 2) there is preliminary evidence that the device is likely to be effective and no significant safety concerns have been identified for the proposed indication.

A copy of the original memorandum dated May 10, 1995 is attached for reference and to provide further elaboration on this policy.

Effective Date

This memorandum is effective immediately.

Susan Alpert, Ph.D., M.D.

Attachment

IDE Memorandum #D96-1
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Date: May 10, 1995

From: Director, Office of Device Evaluation (ODE)

Subject: Investigational Devices Exemption (IDE) Policy Which Permits Continued Access to Investigational Devices While a Marketing Application is Being Prepared or Reviewed

To: ODE Review Staff

It has recently been brought to my attention that the Office policy regarding continued availability of investigational devices during the period between completion of the clinical study and approval of the marketing application requires clarification. In the near future, a blue book memorandum will be developed which will provide specific guidance on this topic. In the mean time, however, ODE's reviewing divisions should use the general principles presented below as a guideline for developing appropriate criteria for their own use.

ODE has traditionally permitted sponsors of clinical investigations to continue to enroll subjects at a pre-determined rate while a marketing application is being prepared by the sponsor or reviewed by the Office if there is: (1) a public health need for the device or (2) if there is preliminary evidence that the device is likely to be effective and no significant safety concerns have been identified for the proposed indication. Such a policy is scientifically sound as it allows the sponsors to collect additional safety and effectiveness data in support of the marketing application or to address new questions regarding the investigational device during this intervening period. This approach is also administratively appropriate as the preparation and review times for a marketing application can be lengthy; and thus, it could be contrary to the public health to prevent access to these potentially safe and effective new devices during a lengthy evaluation period.

Once a preliminary review of the data (IDE, 510(k), or PMA) indicates that there is evidence of safety and effectiveness, a sponsor may propose to conduct an "extended" clinical investigation of the device. An extended investigation may be conducted for a number of reasons. For example, a sponsor may propose an extended trial for the same indication for use as studied under the IDE and use the same study protocol to provide confirmatory evidence of safety and effectiveness. A modified clinical protocol may be used to better define safety and effectiveness in a subpopulation, to support new indications for use or new modalities of use for the device, to identify and quantify adverse reactions, to address long-term effects of the device, to support additional labeling claims, or to confirm that minor changes made to the device design or to the conditions under which the device will ultimately be used do not

substantially impact safety and effectiveness.

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A request for an extended investigation must be submitted by the sponsor of the IDE in writing as a supplement to the IDE. When reviewing a request for an extended investigation from the sponsor, the sponsor's justification for the extension, the preliminary safety and effectiveness data (IDE, 510(k) or PMA), the risks posed by the device, the proposed rate of continued enrollment, the proposed objectives for the extended study, the sponsor's progress toward submission of the marketing application, and/or ODE's progress in the review of the marketing application should be considered. All of these factors may influence ODE's decision to approve, approve with modifications, or disapprove the proposed protocol for this intervening period between completion of the core clinical investigation and approval of the marketing application. The above factors should also be considered by ODE when deciding upon an appropriate rate of enrollment, number of investigators, and number of investigational sites for the study during this stage of product development. Finally, a sponsor who has been negligent in his monitoring responsibilities or who has exhibited other unresolved compliance problems would not be permitted to participate in an extended investigation.

An investigation conducted under the provisions of this policy must still be conducted in accordance with the IDE, IRB, and Informed Consent regulations (21 CFR 812, 56, and 50, respectively). FDA may withdraw approval for the extended investigation for any of the reasons identified in 21 CFR 812.30 (b), if the device is being commercialized, or if there is not satisfactory progression towards submission of the marketing application or towards approval of the marketing application. As in the withdrawal of approval of an IDE, however, ODE must make every attempt to resolve the issue(s) with the sponsor, must notify the sponsor in writing of the issue(s), and must notify the IDE Staff and the Director's office before proceeding with this course of action.

Effective Date

This memorandum is effective immediately.

/s/

Susan Alpert, Ph.D., M.D.

Updated 11/18/1996